HSPB8 gene

heat shock protein family B (small) member 8

Normal Function

The *HSPB8* gene provides instructions for making a protein called heat shock protein beta-8 (also called heat shock protein 22). This protein is a member of the heat shock protein family, which helps protect cells under adverse conditions such as infection, inflammation, exposure to toxins, elevated temperature, injury, and disease. Heat shock proteins block signals that lead to programmed cell death. In addition, they appear to be involved in activities such as cell movement (motility), stabilizing the cell's structural framework (the cytoskeleton), folding and stabilizing newly produced proteins, and repairing damaged proteins. Heat shock proteins also appear to play a role in the tensing of muscle fibers (muscle contraction).

Heat shock protein beta-8 is found in cells throughout the body and is particularly abundant in nerve cells. While its function is not well understood, it seems to interact with a related protein called heat shock protein beta-1, produced from the *HSPB1* gene. In nerve cells, heat shock protein beta-1 helps to organize a network of molecular threads called neurofilaments that maintain the diameter of specialized extensions called axons. Maintaining proper axon diameter is essential for the efficient transmission of nerve impulses. The specific role that heat shock protein beta-8 plays in axons is unclear.

Health Conditions Related to Genetic Changes

Charcot-Marie-Tooth disease

A mutation in the *HSPB8* gene has been reported in more than a dozen individuals in a large Chinese family with a form of Charcot-Marie-Tooth disease known as type 2L. Charcot-Marie-Tooth disease is a group of progressive disorders that affect the peripheral nerves. Peripheral nerves connect the brain and spinal cord to muscles and to sensory cells that detect sensations such as touch, pain, heat, and sound.

The *HSPB8* gene mutation that causes Charcot-Marie-Tooth disease changes the protein building block (amino acid) lysine to the amino acid asparagine at protein position 141, written as Lys141Asn or K141N.

It is unclear how *HSPB8* gene mutations lead to the signs and symptoms of Charcot-Marie-Tooth disease, type 2L. Research suggests that the altered heat shock protein beta-8 interacts more strongly with heat shock protein beta-1 and is more likely to form clumps (aggregates). The aggregates may block the transport of substances that are essential for the proper function of nerve axons.

distal hereditary motor neuropathy, type II

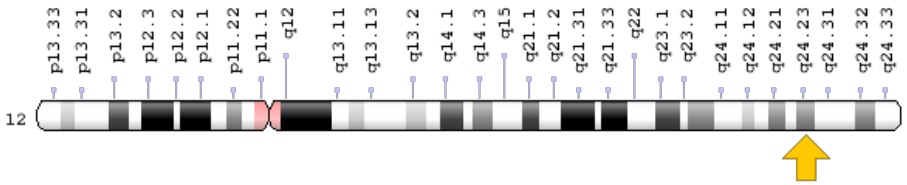
Researchers have identified at least two *HSPB8* gene mutations that cause a condition called distal hereditary motor neuropathy, type II, which is similar to Charcot-Marie-Tooth disease. Distal hereditary motor neuropathy, type II affects peripheral nerves and is characterized by progressive weakness, primarily in the feet and legs. Unlike Charcot-Marie-Tooth disease, distal hereditary motor neuropathy, type II does not affect sensory cells.

One of the *HSPB8* gene mutations that causes distal hereditary motor neuropathy, type II (Lys141Asn or K141N) is also associated with Charcot-Marie-Tooth disease, type 2L. Another mutation replaces the lysine in the same position with glutamic acid (written as Lys141Glu or K141E) and seems to increase protein aggregation in the same way. It is not well understood why the same *HSPB8* gene mutation can cause either disorder. Researchers suggest that different distributions of protein aggregates within the peripheral nerves may result in different patterns of signs and symptoms. The disruption of other cell functions in which this protein is involved may also contribute to peripheral nerve disease.

Chromosomal Location

Cytogenetic Location: 12q24.23, which is the long (q) arm of chromosome 12 at position 24.23

Molecular Location: base pairs 119,178,790 to 119,194,746 on chromosome 12 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- CMT2L
- DHMN2
- E2-induced gene 1
- E2IG1
- H11

- heat shock 22kDa protein 8
- heat shock 27kDa protein 8
- heat shock protein beta-8
- HMN2
- HMN2A
- HSP22
- HspB8
- HSPB8_HUMAN
- protein kinase H11
- small stress protein-like protein HSP22

Additional Information & Resources

GeneReviews

- Charcot-Marie-Tooth Neuropathy Type 2
  https://www.ncbi.nlm.nih.gov/books/NBK1285

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28HSPB8%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- HEAT-SHOCK 22-KD PROTEIN 8
  http://omim.org/entry/608014

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/HSPB8ID43743ch12q24.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=HSPB8%5Bgene%5D
- HGNC Gene Family: Small heat shock proteins
  http://www.genenames.org/cgi-bin/genefamilies/set/585
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=30171

- Inherited Peripheral Neuropathies Mutation Database
  http://www.molgen.ua.ac.be/CMTMutations/Mutations/Mutations.cfm?Context=37
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/26353
- UniProt
  http://www.uniprot.org/uniprot/Q9UJY1

Sources for This Summary

- Dierick I, Baets J, Irobi J, Jacobs A, De Vriendt E, Deconinck T, Merlini L, Van den Bergh P, Rasic VM, Robberecht W, Fischer D, Morales RJ, Mitrovic Z, Seeman P, Mazanec R, Kochanski A, Jordanova A, Auer-Grumbach M, Helderman-van den Enden AT, Wokke JH, Nelis E, De Jonghe P, Timmerman V. Relative contribution of mutations in genes for autosomal dominant distal hereditary motor neuropathies: a genotype-phenotype correlation study. Brain. 2008 May;131(Pt 5):1217-27. doi: 10.1093/brain/awn029. Epub 2008 Mar 5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18325928
- Fontaine JM, Rest JS, Welsh MJ, Benndorf R. The sperm outer dense fiber protein is the 10th member of the superfamily of mammalian small stress proteins. Cell Stress Chaperones. 2003 Spring;8(1):62-9.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12820655
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC514854/
- Fontaine JM, Sun X, Hoppe AD, Simon S, Vicart P, Welsh MJ, Benndorf R. Abnormal small heat shock protein interactions involving neuropathy-associated HSP22 (HSPB8) mutants. FASEB J. 2006 Oct;20(12):2168-70. Epub 2006 Aug 25.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16935933
- GeneReview: Charcot-Marie-Tooth Neuropathy Type 2
  https://www.ncbi.nlm.nih.gov/books/NBK1285
- OMIM: HEAT-SHOCK 22-KD PROTEIN 8
  http://omim.org/entry/608014
- Hu Z, Chen L, Zhang J, Li T, Tang J, Xu N, Wang X. Structure, function, property, and role in neurologic diseases and other diseases of the sHsp22. J Neurosci Res. 2007 Aug 1;85(10):2071-9. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17304582
- Irobi J, Van Impe K, Seeman P, Jordanova A, Dierick I, Verpoorten N, Michalik A, De Vriendt E, Jacobs A, Van Gerwen V, Vennekens K, Mazanec R, Tournev I, Hilton-Jones D, Talbot K, Kremensky I, Van Den Bosch L, Robberecht W, Van Vandekerckhove J, Van Broeckhoven C, Gettemans J, De Jonghe P, Timmerman V. Hot-spot residue in small heat-shock protein 22 causes distal motor neuropathy. Nat Genet. 2004 Jun;36(6):597-601. Epub 2004 May 2.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15122253
- Kasakov AS, Bukach OV, Seit-Nebi AS, Marston SB, Gusev NB. Effect of mutations in the beta5-beta7 loop on the structure and properties of human small heat shock protein HSP22 (HspB8, H11). FEBS J. 2007 Nov;274(21):5628-42. Epub 2007 Oct 8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17922839
- Niemann A, Berger P, Suter U. Pathomechanisms of mutant proteins in Charcot-Marie-Tooth disease. Neuromolecular Med. 2006;8(1-2):217-42. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16775378

- Shemetov AA, Seit-Nebi AS, Gusev NB. Structure, properties, and functions of the human small heat-shock protein HSP22 (HspB8, H11, E2IG1): a critical review. J Neurosci Res. 2008 Feb 1; 86(2):264-9. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17722063
- Tang BS, Zhao GH, Luo W, Xia K, Cai F, Pan Q, Zhang RX, Zhang FF, Liu XM, Chen B, Zhang C, Shen L, Jiang H, Long ZG, Dai HP. Small heat-shock protein 22 mutated in autosomal dominant Charcot-Marie-Tooth disease type 2L. Hum Genet. 2005 Feb;116(3):222-4. Epub 2004 Nov 23.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15565283
- Züchner S, Vance JM. Molecular genetics of autosomal-dominant axonal Charcot-Marie-Tooth disease. Neuromolecular Med. 2006;8(1-2):63-74. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16775367

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